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(54) Title: COSMETIC COMPOSITIONS CONTAINING VITAMIN B_3 COMPOUNDS

(57) Abstract

The present invention relates to topical cosmetic compositions composed primarily of lipophilic materials as the continuous phase and containing vitamin B_3 compounds. Such compositions are useful in improving the stability and skin penetration of compositions containing vitamin B_3 compounds.

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COSMETIC COMPOSITIONS CONTAINING VITAMIN B_3 COMPOUNDS

FIELD OF THE INVENTION

The present invention relates to topical cosmetic compositions composed primarily of lipophilic materials as the continuous phase and containing vitamin B_3 compounds.

BACKGROUND OF THE INVENTION

Niacin, also known as vitamin B_3, is the common name for nicotinic acid. The physiologically active form of niacin is niacinamide, also a member of the vitamin B_3 family of compounds. Niacin and niacinamide (nicotinic acid amide) function in the body as components of two coenzymes: nicotinamide adenine dinucleotide (NAD) and nicotinamide adenine dinucleotide phosphate (NADP). Until recently, these vitamin B_3 compounds were used exclusively to treat niacin deficiency and pellegra.

Today, however, vitamin B_3 compounds have also found use in the area of skin care actives. British Patent 1,370,236 describes compositions for skin lightening containing 0.5% to 10% niacin. Similarly, U.S. Patent 4,096,240 discloses the use of 0.1% to 10% niacinamide for skin lightening. Vitamin B_3 compounds have also been found useful in regulating the texture of human skin. See PCT application WO 97/39733, to Oblong et al. Moreover, the present inventors have found that incorporating solubilized vitamin B_3 compounds into water-in-oil cosmetic carriers improve the penetration of the vitamin B_3 compounds into the skin, thus, enhancing their skin regulating properties.

However, because most vitamin B_3 compounds are soluble in polar solvents, they can pose stability problems when formulated into cosmetic compositions composed primarily of lipophilic materials (i.e., forming a lipophilic continuous phase). When formulating such compositions, the polar solvents (e.g., polyhydric alcohols, water) necessary to dissolve the vitamin B_3 compounds tend to separate from the lipophilic materials, causing the formation of messy looking bulk layers. Moreover, when formulating lipophilic stick compositions (e.g., lipsticks), such phase separation manifests itself as liquid beads along the surface of the stick composition. This can negatively affect consumer acceptability.

Thus, there exists a need for cosmetic compositions comprising vitamin B_3 compounds which provide improved skin penetration of the vitamin B_3 compound and provide good compositional stability. The present inventors have found that the stability of cosmetic compositions comprising a vitamin B_3 compound, a polar solvent and a lipophilic continuous phase can be improved by incorporating surfactant or surfactant mixtures which has a Krafft point at or below about $20^{o}C$ and form association structures such that the association structures thermodynamically bind the moisturizer/polar solvent and homogeneously absorb in the lipophilic matrix.

It is, therefore, an aspect of the present invention to provide cosmetic compositions comprising a lipophilic continuous phase and solubilized vitamin B_3 compounds.

Another aspect of the present invention is to provide cosmetic compositions comprising solubilized vitamin B_3 compounds which provide improved skin penetration of the vitamin B_3 compound.

A further aspect of the present invention is to provide cosmetic stick compositions comprising solubilized vitamin B_3 compounds.

A still further aspect of the present invention is to provide cosmetic stick compositions comprising a lipophilic continuous phase and solubilized vitamin B_3 compounds stabilized by association structures.

Still another aspect of the present invention is to provide cosmetic stick compositions which enhance the penetration of vitamin B_3 compounds into the skin.

These and other aspects will become readily apparent from the detailed description which follows.

SUMMARY OF THE INVENTION

The present invention relates to topical cosmetic compositions useful for providing enhanced skin penetration of a vitamin B3 compound, comprising: from about 0.01% to about 50%, by weight of the composition, of vitamin B_3 compound; from about 1% to about 90%, by weight of the composition, of emollient component comprising from 0.1% to about 100%, by weight of the emollient component, of an oil that is liquid at ambient temperature; from about 0.1% to about 80%, by weight of the composition, of a stabilizing system, comprising: thereof; (i) from about 0.1% to about 90%, by weight of the stabilizing system, of a solidifying agent; and (ii) from about 0.01% to about 30%, by weight of the stabilizing system, of a surfactant, wherein the surfactant has a Krafft point at or below about 20^{o}Cand forms association structures; and from about 0.01% to about 90%, by weight of the composition, of a polar solvent.

All percentages, parts and ratios are based upon the total weight of the cosmetic compositions of the present invention, unless otherwise specified. All such weights as they pertain to listed ingredients are based on the active level and, therefore, do not include carriers or by-products that may be included in commercially available materials, unless otherwise specified.

DETAILED DESCRIPTION OF THE INVENTION

Definition

As used herein, the term "cosmetics" includes make-up, foundation, and skin care products. The term "make-up" refers to products that leave color on the face, including foundation, blacks and browns, i.e., mascara, eye liners, brow colors, eye shadows, blushers, lip colors, and so forth. Skin care products are those used to treat or care for, or somehow moisturize, improve, or clean the skin. Products contemplated by the phrase "skin care products" include, but are not limited to, adhesives, bandages, toothpaste, anhydrous occlusive moisturizers, powder laundry detergent, fabric softener towels, occlusive drug delivery patches, antiperspirants, deodorants, nail polish, powders, tissues, wipes, solid emulsion compact, hair conditioners-anhydrous and the like. The term "foundation" refers to liquid, creme, mousse, pancake, concealer or like product created or reintroduced by cosmetic companies to even out the overall coloring of the skin. Foundation is manufactured to work better over moisturized and/or oiled skin.

As used herein, the term "association structure" refers to an aggregation of surfactant and/or polymer molecules such that they orient themselves forming a composite ordered structure. An association structure is also known in the art as a liquid crystalline phase. A requirement for the formation of a liquid crystal is the hydrocarbon portion of an amphiphilic molecule is transformed into a state with disorder as

that in the liquid state. In spite of the high degree of short-range disorder in these structures there is a long-range order in a least one dimension.

As used herein, the term "solid material" refers to any solidifying ingredient capable of adsorbing the association structures. Solids include waxes, solid fats, clays, fillers, powders, uv-absorbers, suspending agents, waxy emulsifiers or pigments commonly used to thicken or solidify cosmetic compositions.

As used herein, "color(s) or colorants" includes pigments, dyes, colors, lakes, and pearl. Colors are measured on an anhydrous weight basis.

As used herein, the term "lecithin" refers to a material which is a phosphatide. Naturally occurring or synthetic phosphatides can be used. Phosphatidylcholine or lecithin is a glycerine esterified with a choline ester of phosphoric acid and two fatty acids, usually a long chain saturated or unsaturated fatty acid, having 16-20 carbons and up to 4 double bonds. Other phosphatides capable of forming association structures, preferably lamellar or hexagonal liquid crystals, can be used in place of the lecithin or in combination with it. Other phosphatides are glycerol esters with two fatty acids as in the lecithin, but the choline is replaced by ethanolamine (a cephalin), or serine (a-aminopropanoic acid; phosphatidyl serine) or an inositol (phosphatidyl inositol).

As used herein, the term "surfactant" refers to a low molecular weight or monomer non-polymeric organic compound amphiphilic in nature, i.e., it has hydrophilic and hydrophobic groups and exhibits a marked tendency to adsorb on a surface or interface and lower the surface tension. Surfactants or emulsifiers are divided into nonionic (no charge), anionic (negative charge), cationic (positive charge) and amphoteric (both charges) based on whether or not they ionize in aqueous media. Surfactants are monomers and are derived from natural oils and fats and crude oils. The term "surfactant" as used herein refers to mixtures of surfactants as well as a single organic compound.

As used herein, "polar solvent" means a polar material capable of forming an association structure with a surfactant. Some examples of polar solvents include glycerine, panthenol (preferably panthenol mixed with glycerine or alcohol), propylene glycol, butylene glycol, hexylene glycol, water, alcohols, alkanediols, polyethylene glycols, sorbitol, maltilal and mixtures thereof.

As used herein the term "comprising" means that the composition can contain other ingredients which are compatible with the composition and which preferably do not substantially disrupt the association structures of the present invention. The term encompasses the terms "consisting of" and "consisting essentially of".

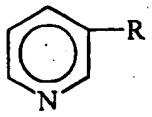
As used herein, the term "ambient temperature" refers to the temperature also known in the art as "room temperature" and typically means about 20°C. Generally ambient temperature can range from about 18°C to about 27°C, preferably from about 20°C to about 25°C, depending on such variables as geographical location, i.e. sub-tropical vs. temperate regions.

ESSENTIAL COMPONENTS

Vitamin B_3 Component

The compositions of the present invention comprise a safe and effective amount of a natural or synthetic vitamin B_3 compound. The compositions of the present invention preferably comprise from above 0.01% to about 50%, more preferably from about 0.1% to about 30%, even more preferably 0.5% to about 20%, most preferably from about 1% to about 10% of the vitamin B_3 compound.

As used herein, "vitamin B_3 compound" means a compound having the formula:



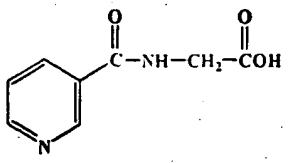
wherein R is - $CONH_2$ (i.e., niacinamide), - COOH (i.e., nicotinic acid) or - CH_2OH (i.e., nicotinyl alcohol); derivatives thereof; and salts of any of the foregoing.

Exemplary derivatives of the foregoing vitamin B_3 compounds include nicotinic acid esters, including non-vasodilating esters of nicotinic acid, nicotinyl amino acids, nicotinyl alcohol esters of carboxylic acids, nicotinic acid N-oxide and niacinamide N-oxide.

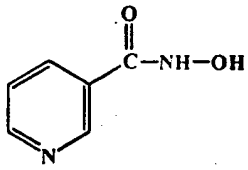
Suitable esters of nicotinic acid include nicotinic acid esters of C_1-C_{22}, preferably C_1-C_{16}, more preferably C_1-C_6 alcohols. The alcohols are suitably straight-chain or branched chain, cyclic or acyclic, saturated or unsaturated (including aromatic), and substituted or unsubstituted. The esters are preferably non-rubifacient. As used herein, "non-rubifacient" means that the ester does not commonly yield a visible flushing response after application to the skin in the subject compositions (the majority of the general population would not experience a visible flushing response, although such compounds may cause vasodilation not visible to the naked eye). Alternatively, a nicotinic acid material which is rubifacient at higher doses could be used at a lower dose to reduce the rubifacient effect. Non-rubifacient esters of nicotinic acid include tocopherol nicotinate and inositol hexanicotinate; tocopherol nicotinate is preferred.

Other derivatives of the vitamin B_3 compound are derivatives of niacinamide resulting from substitution of one or more of the amide group hydrogens. Nonlimiting examples of derivatives of niacinamide useful herein include nicotinyl amino acids, derived, for example, from the reaction of an activated nicotinic acid compound (e.g., nicotinic acid azide or nicotinyl chloride) with an amino acid, and nicotinyl alcohol esters of organic carboxylic acids (e.g., C1 - C18). Specific examples of such derivatives include nicotinuric acid and nicotinyl hydroxamic acid, which have the following chemical structures:

nicotinuric acid:



nicotinyl hydroxamic acid:



Exemplary nicotinyl alcohol esters include nicotinyl alcohol esters of the carboxylic acids salicylic acid, acetic acid, glycolic acid, palmitic acid and the like. Other non-limiting examples of vitamin B_3 compounds useful herein are 2-chloronicotinamide, 6-aminonicotinamide, 6-methylnicotinamide, n-methyl-nicotinamide, n,n-diethylnicotinamide, n-(hydroxymethyl)-nicotinamide, quinolinic acid imide, nicotinanilide, n-benzylnicotinamide, n-ethylnicotinamide, nifenazone, nicotinaldehyde, isonicotinic acid, methyl isonicotinic acid, thionicotinamide, nialamide, 1-(3-pyridylmethyl) urea, 2-mercaptonicotinic acid, nicomol, and niaprazine.

Examples of the above vitamin B_3 compounds are well known in the art and are commercially available from a number of sources, e.g., the Sigma Chemical Company (St. Louis, MO); ICN Biomedicals, Inc. (Irvin, CA) and Aldrich Chemical Company (Milwaukee, WI).

One or more vitamin B_3 compounds may be used herein. Preferred vitamin B_3 compounds are niacinamide and tocopherol nicotinate. Niacinamide is more preferred.

When used, salts, derivatives, and salt derivatives of niacinamide are preferably those having substantially the same efficacy as niacinamide in the methods of regulating skin condition described herein.

Salts of the vitamin B_3 compound are also useful herein. Nonlimiting examples of salts of the vitamin B_3 compound useful herein include organic or inorganic salts, such as inorganic salts with anionic inorganic species (e.g., chloride, bromide, iodide, carbonate, preferably chloride), and organic carboxylic acid salts (including mono-, di- and tri- C1 - C18 carboxylic acid salts, e.g., acetate, salicylate, glycolate, lactate, malate, citrate, preferably monocarboxylic acid salts such as acetate). These and other salts of the vitamin B_3 compound can be readily prepared by the skilled artisan, for example, as described by W. Wenner, "The Reaction of L-Ascorbic and D-Isoascorbic Acid with Nicotinic Acid and Its Amide", J. Organic Chemistry, VOL. 14, 22-26 (1949), which is incorporated herein by reference. Wenner describes the synthesis of the ascorbic acid salt of niacinamide.

In a preferred embodiment, the ring nitrogen of the vitamin B_3 compound is substantially chemically free (e.g., unbound and/or unhindered), or after delivery to the skin becomes substantially chemically free ("chemically free" is hereinafter alternatively referred to as "uncomplexed"). More preferably, the vitamin B_3 compound is essentially uncomplexed. Therefore, if the composition contains the vitamin B_3 compound in a salt or otherwise complexed form, such complex is preferably substantially reversible, more preferably essentially reversible, upon delivery of the composition to the skin. For example, such complex should be substantially reversible at a pH of from about 5.0 to about 6.0. Such reversibility can be readily determined by one having ordinary skill in the art.

More preferably the vitamin B_3 compound is substantially uncomplexed in the composition prior to delivery to the skin. Exemplary approaches to minimizing or preventing the formation of undesirable complexes include omission of materials which form substantially irreversible or other complexes with the vitamin B_3 compound, pH adjustment, ionic strength adjustment, the use of surfactants, and formulating wherein the vitamin B_3 compound and materials which complex therewith are in different phases. Such approaches are well within the level of ordinary skill in the art.

Thus, in a preferred embodiment, the vitamin B_3 compound contains a limited amount of the salt form and is more preferably substantially free of salts of a vitamin B_3 compound. Preferably the vitamin B_3 compound contains less than about 50% of such salt, and is more preferably essentially free of the salt form. The vitamin B_3 compound in the compositions hereof having a pH of from about 4 to about 7 typically contain less than about 50% of the salt form.

The vitamin B_3 compound may be included as the substantially pure material, or as an extract obtained by suitable physical and/or chemical isolation from natural (e.g., plant) sources. The vitamin B_3 compound is preferably substantially pure, more preferably essentially pure.

Vitamin B_3 compounds which exist in crystalline form are particularly preferred for use herein.

Emollient Component

The compositions of the present invention further comprise an emollient component, suitable for suspending or otherwise dispersing the crystalline vitamin B_3 compound therein. Any emollient that is known or otherwise suitable for use in cosmetic applications, and which is also compatible with the vitamin B_3 compound in the composition, may be used in the composition of the present invention.

Preferred emollients for use in the composition of the present invention are those materials referred to in the personal care arts as fats, oils, fatty alcohols, fatty acids, esters of fatty acids, and combinations thereof, and which aid application and adhesion, yield gloss and most importantly provide occlusive moisturization.

Suitable emollients for use in compositions of the present invention are isostearic acid derivatives, isopropyl palmitate, lanolin oil, diisopropyl dimerate, maleated soybean oil, octyl palmitate, isopropyl isostearate, cetyl lactate, cetyl ricinoleate, tocopheryl acetate, acetylated lanolin alcohol, cetyl

acetate, phenyl trimethicone, glyceryl oleate, tocopheryl linoleate, wheat germ glycerides, arachidyl propionate, myristyl lactate, decyl oleate, propylene glycol ricinoleate, isopropyl lanolate, pentaerythrityl tetrastearate, neopentylglycol dicaprylate/dicaprate, hydrogenated coco-glycerides, isononyl isononanoate, isotridecyl isononanoate, myristal myristate, triisocetyl citrate, cetyl alcohol, octyl dodecanol, oleyl alcohol, panthenol, lanolin alcohol, linoleic acid, linolenic acid, sucrose esters of fatty acids, octyl hydroxystearate and mixtures thereof. Examples of other suitable emollients can be found in the Cosmetic Bench Reference, pp. 1.19-1.22 (1996), which descriptions are incorporated herein by reference.

Suitable oils for use in compositions of the present invention include esters, triglycerides, hydrocarbons and silicones. These can be a single material or a mixture of one or more materials. They will normally comprise from 0.1% to about 100%, preferably from about 5% to about 90%, and most preferably from about 70% to about 90% of the emollient component.

Oils act as emollients and also impart viscosity, tackiness, and drag properties to cosmetic compositions such as lipsticks. Examples of suitable oils include caprylic triglycerides; capric triglyceride; isostearic triglyceride; adipic triglyceride; propylene glycol myristyl acetate; lanolin; lanolin oil; polybutene; isopropyl palmitate; isopropyl myristate; isopropyl isostearate; diethyl sebacate; diisopropyl adipate; tocopheryl acetate; tocopheryl linoleate; hexadecyl stearate; ethyl lactate; cetyl oleate; cetyl ricinoleate; oleyl alcohol; hexadecyl alcohol; octyl hydroxystearate; octyl dodecanol; wheat germ oil; hydrogenated vegetable oils; castor oil; petrolatum; modified lanolins; branched-chain hydrocarbons; alcohols and esters; corn oil; cottonseed oil; olive oil; palm kernel oil; rapeseed oil; safflower oil; jojoba oil; evening primrose oil; avocado oil mineral oil, sheabutter, octylpalmitate, maleated soybean oil, glycerol trioctanoate, diisopropyl dimerate, and volatile and non-volatile silicone oils including phenyl trimethicone.

The preferred oils for use herein are acetylglycerides, octanoates, and decanoates of alcohols and polyalcohols, such as those of glycol and glycerol, the ricinoleates of alcohols and polyalcohols such as cetyl ricinoleate, PG-3 diisostearate, polyglycerol ethers, polyglycerol esters, caprylic triglycerides, capric triglycerides, isostearic triglyceride, adipic triglyceride, phenyl trimethicone, lanolin oil, polybutene, isopropyl palmitate, isopropyl isostearate, cetyl ricinoleate, octyl dodecanol, oleyl alcohol, hydrogenated vegetable oils, castor oil, modified lanolins, octyl palmitate, lanolin oil, maleated soybean oil, cetyl ricinoleate, glyceryl trioctanoate, diisopropyl dimerate, synthetic lanolin derivatives and branched chain alcohols, sucrose esters of fatty acids, octyl hydroxystearate and mixtures thereof.

Preferably, the oils used are selected such that the majority (at least about 75%, preferably at least about 80% and most preferably at least about 99%) of the types of oils used have solubility parameters which do not differ by more than from about 1 to about 0.1, preferably from about 0.8 to about 0.1.

The emollient component comprises from about 1% to about 90%, preferably from about 10% to about 80%, more preferably from about 20% to about 70%, and most preferably from about 40% to about 60%, of the cosmetic composition.

Stabilizing System

The compositions of the present invention further comprise a stabilizing system. The phrase "stabilizing system," as used herein means a system which prevents the coalescence of polar solvent droplets and/or, in the case of stick compositions, their migration to the surface of the stick.

a.) Solidifying Agent

The cosmetic compositions of this invention can contain one or more materials, herein singly or collectively referred to as a " solidifying agent" , that are effective to solidify the particular liquid base materials to be used in a cosmetic composition. (As used herein, the term "solidify" refers to the physical and/or chemical alteration of the liquid base material so as to form a solid or semi-solid at ambient conditions, i.e., to form a final composition which has a stable physical structure and is deposited on the skin during normal use conditions.) As is appreciated by those skilled in the art, the selection of the particular solidifying agent for use in the cosmetic compositions will depend upon the particular type of composition desired, i.e., gel or wax-based, the desired rheology, the liquid base material used and the other materials to be used in the composition. The solidifying agent is preferably present at a concentration of from about 0.1% to about 90%, more preferably from about 1 to about 50%, even more preferably from about 5% to about 40%, most preferably from about 3% to about 20%.

The wax cosmetic stick embodiments of this invention preferably contain from about 5% to about 50% (by weight) of a waxy solidifying agent. By the term "waxy solidifying agent," as used herein, is meant a solidifying material having wax-like characteristics. Such waxy materials may also serve as emollients. Among the waxy materials useful herein are the high melting point waxes, i.e., having a melting point of from about 65°C to about 125°C, such as beeswax, spermaceti, carnauba, baysberry, candelilla, montan, ozokerite, ceresin, paraffin, synthetic waxes such as Fisher-Tropsch waxes, microcrystalline wax, and mixtures thereof. Ceresin, ozokerite, white beeswax, synthetic waxes, and mixtures thereof, are among the preferred high-melting point waxes useful herein. Compositions containing waxes among those useful herein are disclosed in U.S. Patent 4,049,792, Elsnau, issued Sept. 20, 1977, herein incorporated by reference in its entirety). Low melting waxes, having a melting point of from about 37°C to about 75°C, are preferred for use in the wax stick embodiments of this invention. Wax stick embodiments of this invention, which contain volatile silicone oils as a liquid base material, preferably contain from about 10% to about 35%, more preferably from about 10% to about 20% (by weight), of a low-melting wax. Such materials include fatty acids, fatty alcohols, fatty acid esters and fatty acids amides, having fatty chains of from about 8 to about 30 carbon atoms, and mixtures thereof. Preferred wax-like materials include cetyl alcohol, palmitic acid, stearyl alcohol, behenamide, sucrose esters of tallow fatty acids, mono and di-fatty acid esters of polyethylene glycol, and mixtures thereof. Stearyl alcohol, cetyl alcohol, and mixtures thereof, are particularly preferred. Fatty acids, fatty alcohols, and other wax-like materials useful in this invention are also disclosed in the following references, all of which are incorporated by reference herein: U.S. Patent 4,151,272, Geary, et al., issued Apr. 24, 1979; U.S. Patent 4,229,432, Geria, issued Oct. 21, 1980; and U.S. Patent 4,280,994, Turney, issued July 28, 1981; "The

Chemistry and Technology of Waxes", A. H. Warth, 2nd Edition, reprinted in 1960, Reinhold Publishing Corporation, pp 391-393 and 421; "The Petroleum Chemicals Industry", R. F. Goldstein and A. L. Waddeam, 3rd Edition (1967), E & F. N. Span Ltd., pp 33-40; "The Chemistry and Manufacture of Cosmetics", M. G. DeNavarre, 2nd edition (1970), Van Nostrand & Company, pp 354-376; and in "Encylopedia of Chemical Technology:, Vol. 24, Kirk-Othmer, 3rd Edition (1979) pp 466-481. Preferred wax-like materials useful as solidifying agents in the present wax sticks are described in U.S. Patent 4,126,679, Davy, et al., issued Nov. 21, 1978, herein incorporated by reference in its entirety. Preferred mixtures of wax-like materials comprise fatty alcohols containing carbon chains of from about 14 to about 18 carbon atoms, and alcohols having chain lengths of 20 carbons or longer, wherein the final mixture contains from about 1% to about 3% (by weight) of the longer-chain fatty alcohols. Compositions containing these fatty alcohol mixtures are described in European Patent Specification No. 117,070, May, published Aug. 29, 1984 (incorporated by reference herein).

Also useful herein are biopolymers such as those described in European Application No. 522624, to Dunphy et al., herein incorporated by reference in its entirety.

The gel stick embodiments of this invention preferably contain from about 3% to about 30%, preferably from about 3% to about 10% (by weight), of a solidifying agent. The particular amount of solidifying agent to be used will depend upon the particular solidifying agent and the liquid base material used, and the desired physical characteristics of the gel stick. Solidifying agents useful in the gel stick embodiments of this invention are, in general, surface-active compounds which form networks immobilizing or solidifying the liquid base materials into a gel. Such solidifying agents include: soaps, such as the sodium and potassium salts of higher fatty acids, i.e., acids having from 12 to 22 carbon atoms; amides of higher fatty acids; higher fatty acid amides of alkylolamines; dibenzaldehyde-monosorbitol acetals; alkali metal and alkaline earth metal salts of the acetates, propionates and lactates; waxes, such as candelilla and carnauba waxes; and mixtures thereof. Among those solidifying agents preferred for use in the gel stick embodiments of this invention are sodium stearate, sodium palmitate, aluminum stearate, aluminum magnesium hydroxy stearate, and mixtures thereof. Gel stick compositions containing solidifying agents among those useful herein are described in the following patent documents, all incorporated herein by reference in their entirety: U.S. Patent 2,900,306, Slater, issued Aug. 18, 1959; U.S. Patent 3,255,082, Barton, issued June 7, 1966; U.S. Patent 4,137,306, Rubino, et al., issued Jan. 30, 1979; U.S. Patent 4,154,816, Roehl, et al., issued May 15, 1979; U.S. Patent 4,226,889, Yuhas, issued Oct. 7, 1980; U.S. Patent 4,346,079, Roehl, issued Aug. 24, 1982; U.S. Patent 4,383,988, Teng, et al., issued May 17, 1983; European Patent Specification No. 107,330, Luebbe, et al., published May 2, 1984; and U.S. patent application Ser. No. 630,790, DiPietro, filed July 13, 1984. Preferred solidifying agents useful in the gel stick embodiments of the present invention are described in European Patent Specification No. 24,365 Sampson, et al., published Mar. 4, 1981, incorporated herein by reference in its entirety.

Also useful herein as solidifying agents are conventional thickening agents. Examples of suitable thickeners include, but are not limited to, naturally-occurring polymeric materials such as, locust bean gum,

sodium alginate, sodium caseinate, egg albumin, gelatin agar, carrageenin gum sodium alginate, xanthan gum, quince seed extract, tragacanth gum, starch, chemically modified starches and the like, semi-synthetic polymeric materials such as cellulose ethers (e.g. hydroxyethyl cellulose, methyl cellulose, carboxymethyl cellulose, hydroxy propylmethyl cellulose), polyvinylpyrrolidone, polyvinylalcohol, guar gum, hydroxypropyl guar gum, soluble starch, cationic celluloses, cationic guars and the like and synthetic polymeric materials such as carboxyvinyl polymers, polyvinylpyrrolidone, polyvinyl alcohol polyacrylic acid polymers, polymethacrylic acid polymers, polyvinyl acetate polymers, polyvinyl chloride polymers, polyvinylidene chloride polymers and the like. Inorganic thickeners may also be used such as aluminium silicates, such as, for example, bentonites, or a mixture of polyethylene glycol and polyethylene glycol stearate or distearate. Naturally occurring polymers or biopolymers and their use are further described in European Application No. 522624, to Dunphy et al. Additional examples of naturally occurring polymers or biopolymers can be found in the Cosmetic Bench Reference, pp. 1.40-1.42, herein incorporated by reference.

Also useful herein as solidifying agents are hydrophilic gelling agents such as the acrylic acid/ethyl acrylate copolymers and the carboxyvinyl polymers sold by the B.F. Goodrich Company under the trademark of Carbopol Registered TM resins. These resins consist essentially of a colloidally water-soluble polyalkenyl polyether crosslinked polymer of acrylic acid crosslinked with from 0.75% to 2.00% of a crosslinking agent such as polyallyl sucrose or polyallyl pentaerythritol. Examples include Carbopol 934,Carbopol 940, Carbopol 950, Carbopol 980, Carbopol 951 and Carbopol 981. Carbopol 934 is a water-soluble polymer of acrylic acid crosslinked with about 1% of a polyallyl ether of sucrose having an average of about 5.8 allyl groups for each sucrose molecule. Also suitable for use herein are carbomers sold under the Trade Name "Carbopol Ultrez 10, Carbopol ETD2020, Carbopol 1382, Carbopol 1342 and Pemulen TR-1 (CTFA Designation: Acrylates/10-30 Alkyl Acrylate Crosspolymer). Combination of the above polymers are also useful herein. Other gelling agents suitable for use herein include oleogels such as trihydroxystearin.

Hydrophobically modified celluloses are also suitable for use herein as solidifying agents. These celluloses are described in detail in U.S. Patents 4,228,277 and 5,104,646, both of which are herein incorporated by reference in their entirety.

Additional examples of suitable gelling agents or gellants can be found in the Cosmetic Bench Reference, p. 1.27, herein incorporated by reference.

Without being limited by theory, the solidifying agent in combination with the emollient is believed to act as an occlusive on the skin by forming continuous or discontinuous bi-layer or multi-layer films on the skin. The term "occlusive," as used herein, means a preventing or obstructing something, in this case, preventing the removal of moisture (via evaporation) and the vitamin B_3 compound (via film binding) from the surface of the skin.

b.) Surfactant

The compositions of the present invention further comprise a surfactant. Surfactants suitable for use in the compositions of the present invention, are those which can form association structures, preferably lamellar liquid crystals or reverse hexagonal, at ambient temperature when mixed with a polar solvent. Ambient temperature/room temperature as used herein typically means about 20°C. Generally ambient temperature can range from about 18°C to about 27°C, preferably from about 20°C to about 25°C, depending on such variables as geographical location, i.e. sub-tropical vs. temperate regions. One of ordinary skill in the art is able to determine if association structures form at ambient temperatures. The surfactants suitable for use generally have a Krafft point at or below about ambient temperature about 20°C or generally at or below about 18°C to about 27°C, preferably at or below from about 20°C to about 25°C.

The definition of Krafft point is well known in the art and one of ordinary skill in the art can determine a surfactant's Krafft point. In general terms, Krafft point is the melting point of the hydrocarbon chains of the surfactants. It can also be expressed as the temperature at which the solubility of an association colloid in water suddenly increases because critical micelle concentration is exceeded and micelles form. See Ekwall., P., "Composition, Properties and Structure of Liquid Crystalline Phases in Systems of Amphiphilic Compounds" Advances in Liquid Crystals Vol. I, Chapter I, p.81.

In preparing a sample combination of surfactant and polar solvent to demonstrate the ability to form association structures, the surfactant needs to be sufficiently soluble in the polar solvent such that an association structure can form at ambient temperature. One of ordinary skill in the art is capable of determining compatible interactions.

Any surfactant which forms association structures at ambient temperature and is suitable for use in cosmetics is suitable for use herein. Surfactants suitable for use in cosmetics do not present dermatological or toxicological problems. Anionic surfactants, nonionic surfactants, cationic surfactants, amphoteric surfactants and mixtures thereof are suitable for use. Preferably anionic surfactants, nonionic surfactants, cationic surfactants, amphoteric surfactants and mixtures thereof having a Krafft point at or below about ambient temperature are used. More preferably, nonionic surfactants, cationic surfactants, amphoteric surfactants and mixtures thereof having a Krafft point at or below about ambient temperature are used.

Surfactants suitable for use herein are found in U.S. Patent 5,843,407 to El-Nokaly, herein incorporated by reference.

The association structures of the present invention are also useful in improving the skin penetration of the vitamin B_3 compound. Without being limited by theory, the association structures are believed to act either as an occlusive or entrapping matrix on the skin by forming continuous or discontinuous bi-layer or multi-layer films on the skin. The term "occlusive," as used herein, means a preventing or obstructing something, in this case, preventing the removal of moisture (via evaporation) and the vitamin B_3 compound (via film binding) from the surface of the skin. The term "entrapping matrix" as used herein, refers to unilamellar, multilamellar vesicles, cylindrical micelles, hexagonal

liquid crystals, lamellar liquid crystals, or cubic phase liquid crystals capable of binding to the skin. The entrapping matrix entraps the vitamin B_3 compound and, thus, maintains skin contact with the vitamin B_3 compound. Furthermore, since the association structures of the present invention are thermodynamically stable, it is believed that the entrapped or bound polar solvent is slowly released over time. The slow release of the polar solvent thereby aids in maintaining the vitamin B_3 compound in solubilized form, thus, improving skin penetration of the vitamin B_3 compound. The occlusive effect is even further enhanced by the addition of the waxy or wax-like (or gel-like) solidifying agents disclosed above.

The surfactants can be used at levels from about 4% to about 97%, preferably from about 5% to about 95%, more preferably from about 20% to about 90% and most preferably from about 30% to about 70% of the association structure.

Polar Solvent

The solvents useful for making the association structures of the present invention include any polar solvent. In general, "polar solvents" refers to those solvents that contain hydroxyl and/or carbonyl groups and also have high dielectric constants and strong polarity. Suitable polar solvents include: water; alcohols, such as ethanol, propyl alcohol, isopropyl alcohol, hexanol, and benzyl alcohol; polyols, such as propylene glycol, polypropylene glycol, butylene glycol, hexylene glycol, maltitol, sorbitol, and glycerine; panthenol dissolved in glycerine; flavor oils, and mixtures thereof. Mixtures of these solvents can also be used. Preferred polar solvents are polyhydric alcohols and water. Examples of preferred solvents include glycerine, panthenol in glycerine, glycols such as propylene glycol and butylene glycol, polyethylene glycols, water and mixtures thereof. The most preferred polar solvents for use are alcohols, glycerine, panthenol, propylene glycol, butylene glycol and mixtures thereof.

The cosmetic compositions of the present invention will comprise from about 0.01% to about 90%, preferably from about 0.1% to about 60%, more preferably from about 1% to about 30% and most preferably from about 3% to about 18% by weight of the composition of polar solvent. Preferably, the solvents are used in relation to the association structures atlevels of from about 3% to about 96%, preferably from about 5% to about 95%, more preferably from about 10% to about 80% and most preferably from about 30% to about 70% by weight of the association structure.

Preparation of the Association Structure

Formation of the association structure, i.e., cylindrical reverse micelles and/or liquid crystals and the concentration at which such association structures occur is dependent upon a variety of factors, including the specific types of surfactant, solvent, temperature, solubility of the surfactant in the solvent, and concentration of the surfactant in the carrier. The purity of the surfactant affects the concentration level at which the association structures and particularly the preferred form of lamellar liquid crystals form.

The polar solvent and surfactant are mixed together. Formation of the association structure, particularly the preferred lamellar or hexagonal liquid crystalline state is accelerated by mechanical agitation. Mixing, can be performed either by hand (i.e., using hand utensils) or with mechanical

equipment useful for home, institutional, or industrial cosmetic preparation. Extruders which provide a shearing operation with mixing can be used.

The one-phase liquid crystal is most preferred. It is preferred that a substantially two phase liquid crystal, one-phase liquid crystal or single phase liquid crystal component of (preferably at least 90%) be utilized.

Separation and thus detection of the association structure from excess liquid (solvent or solution) or solid may be achieved by ultracentrifugation. Ultracentrifugation should be conducted using sufficiently high centrifugal forces (preferably within the range of from about 20,000 rpm to about 60,000 rpm for from about one hour to about sixteen hours utilizing a Beckman L8-80 centrifuge equipped with a SW60Ti Rotor or by applying about 300,000*g for about one hour) to induce the formation of observable phase boundaries over a period of time. Under these conditions a good separation of the individual phases is obtained. The volume of each phase is determined by calibration of the centrifuge tube and the volume fraction of the individual phase thus calculated.

Optionally, the compositions of the present invention may also include additional colloidal structures. Nonlimiting examples of such colloid structures emulsions and gel networks. A detailed description of these and other useful colloid structures is found in Niels J. Krog, Food Emulsifiers, pp. 141-188, Marcel Dekker, Inc., (1997), herein incorporated by reference in its entirety.

OPTIONAL COMPONENTS

Color

Certain embodiments of the present invention, preferably lipsticks or lip paints, may further comprise from about 0.1% to about 90%, preferably from about 1% to about 35%, more preferably from about 1% to about 20% and most preferably from about 5% to about 15%, of color, on an anhydrous pigment weight basis. These are usually aluminum, barium or calcium salts or lakes. Preferably, dyes are present at from about 0.1% to about 4% and pearls from 0% to about 20%.

Pigments are typically dispersed in emollients for the good dispersion of the pigments when incorporated into the lip compositions, thus providing an even distribution of color. Excellent dispersion of the pigment can be achieved by utilizing association structures, preferably lamellar liquid crystals, as a means of incorporating the color/pigments into the cosmetic compositions of the present invention. A preferred method of incorporating dry pigments comprises the steps of:

(a) preparing a mixture consisting essentially of:

(1) a polar solvent; and

(2) a surfactant selected from the group consisting of amphoteric, cationic, anionic and nonionic surfactants having a Krafft point at or below about ambient temperature and mixtures thereof; and

(b) stirring said mixture until association structures form;

(c) adding and mixing dry pigments until achieving a homogenous mixture;

(d) milling said mixture until uniform particle size is achieved; and

(e) adding and mixing the mixture of (c) to the remaining ingredients until a homogenous mixture is obtained.

If the ingredients of the cosmetic composition are being processed such that the association structures are being formed in situ, the preferred method of incorporating the dry pigments is to slurry them in one or more of the liquid emollient ingredients.

Colors/pigments suitable for use herein are all inorganic and organic colors/pigments suitable for use in lipstick compositions.

Lakes are either a pigment that is extended or reduced with a solid diluent or an organic pigment that is prepared by the precipitation of a water-soluble dye on an adsorptive surface, which usually is aluminum hydrate. There is uncertainty in some instances as to whether the soluble dye precipitates on the surface of the aluminum hydrate to yield a dyed inorganic pigment or whether it merely precipitates in the presence of the substrate. A lake also forms from precipitation of an insoluble salt from an acid or basic dye. Calcium and barium lakes are also used herein.

Lakes suitable for use in the present invention include Red 3 Aluminum Lake, Red 21 Aluminum Lake, Red 27 Aluminum Lake, Red 28 Aluminum Lake, Red 33 Aluminum Lake, Yellow 5 Aluminum Lake, Yellow 6 Aluminum Lake, Yellow 10 Aluminum Lake, Orange 5 Aluminum Lake and Blue 1 Aluminum Lake, Red 6 Barium Lake, Red 7 Calcium Lake.

Other colors and pigments can also be included in the lipsticks, such as dyes and pearls, titanium oxides, Red 6, Red 21, Brown, Russet and Sienna dyes, chalk, talc, iron oxides and titanated micas.

Preferably, the color component is water-insoluble particulate solids having an average primary particle size diameter of less than about 5 microns, preferably 2 microns, more preferably 1 microns.

Without being limited by theory, it is believed that such solid particulates position themselves at the interface of dispersed droplets (i.e., the discontinuous phase) and the continuous phase to serve as barriers, preventing the coalescence of the dispersed droplets and, hence, improving stabilization. A more detailed explanation of this phenomenon is described in S. E. Friberg and Kåre Larsson, Food Emulsions, pp. 36-41, Marcel Dekker, Inc. (1997), herein incorporated by reference in its entirety.

Dispersants may also be used in conjunction with the colors and pigments of the present invention. Examples of suitable dispersants include, but are not limited to, those described in U.S. Patent 5,688,493, herein incorporated by reference in its entirety.

Other Additives

Other optional ingredients which can be present in the cosmetic compositions of the present invention include the flavor oils,, fat soluble vitamins such as vitamin A and E, esters of vitamin A (e.g., acetate, propionate, or palmitate) and of vitamin E (e.g., acetate or sorbate), sunscreens such as octyl methoxycinnamate, butyl methoxydibenzoylmethane, titanium dioxide and zinc oxide, germicides such as triclosan, anti-inflammatory agents such as hydrocortisone, lipid materials such as ceramides and liposomes and skin care actives. The cosmetic compositions can comprise ingredients conventionally

employed in cosmetic compositions such as mascara, foundation or lipcare products. This includes skin care active ingredients such as pharmaceutically active ingredients.

Skin care actives ingredients in both water soluble and water insoluble forms can be added to the cosmetic compositions of the present invention. These include, but are not limited to vitamin C and its derivatives (e.g., ascorbyl palmitate, ascorbyl phosphate and its salts such as magnesium or sodium), vitamin D, panthenol, retinoic acid, zinc oxide, beta-glycyerhetic acid; chamomile oil; ginko biloba extract; pyroglutamic acid, salts or esters; sodium hyaluronate; 2-hydroxyoctanoic acid; sulfur; salicylic acid; carboxymethyl cysteine, and mixtures thereof.

These additives, both fat soluble and water soluble, will normally be present in amounts of less than about 10% by weight, and generally in the range of about 0.01% to about 5%, preferably from about 0.01% to about 3%, most preferably from about 0.1% to about 1%, by weight.

Flavor oils such as peppermint oil, orange oil, citrus oil, wintergreen oil can be used along with an alcohol or glycerine. Flavor oils are usually mixed in a solvent such as ethanol to dilute the flavor. The flavor oils useful herein can be derived from natural sources or be synthetically prepared. Generally flavor oils are mixtures of ketones, alcohols, fatty acids, esters and terpenes. The term "flavor oil" is generally recognized in the art to be a liquid which is derived from botanical sources, i.e. leaves, bark, or skin of fruits or vegetables, and which are usually insoluble in water. The level of flavor oil used can range from 0% to about 5%, preferable from 0% to about 1%.

Additional moisturizers may also be included into the present compositions. Preferred moisturizers include pyrrolidone carboxylic acid, sodium lactate or lactic acid, urea, guanidine, glyceric acid and its salts (e.g., calcium salt), petrolatum, collagen, α-hydroxy propylglyceryl ether, α-hydroxy acids (e.g., ethylglycolic acid, leucic acid, mandelic acid, glycolic acid), glucosamines, and elastin fibers, D-panthenol, allantoin and hyaluronic acid and chondroitin sulfate. Examples of suitable moisturizers can be found in Cosmetic Bench Reference, p. 1.30-1.32 (1996), herein incorporated by reference.

Also useful herein are emulsifiers commonly known as coupling agents can also be used herein. The overall concentration of the emulsifier can be from 0% to about 20% of the formulation, preferably from 0% to about 15% and most preferably from about 1% to about 10%. Examples of suitable emulsifiers can be found in U.S. Patent 5,085,856 to Dunphy et al.; Japanese Patent Publication Sho 61-83110; European Patent Application EP 522624 to Dunphy et al.; U.S. patent 5,688,831 to El-Nokaly et al.; and Examples of suitable moistures can be found in Cosmetic Bench Reference, pp. 1.22, 1.24-1.26 (1996), all of which are herein incorporated by reference in their entirety.

A preferred embodiment of the present invention preferably comprises: a.) from about 1% to about 10%, niacinamide, b.) from about 0.1% to about 50%, preferably from about 0.1% to about 15%, polar solvent c.) from about 0.1% to about 20%, surfactants of the cosmetic composition and d) from about 0.1% to about 50% of an oil that is liquid at ambient temperature. The surfactants are preferably a mixture wherein from about 50% to about 75% of the mixture is made up of surfactants which have a Krafft point of at or below about ambient temperature and form association structures at ambient

temperature and from about 25% to about 50% of the mixture is made up of surfactants which are coupling agents. Another preferred mixture of surfactants which can form association structures and surfactants which act as coupling agent is lecithin, PG-3 diisosterate, sorbitan monooleate, cholesterol 12 hydroxystearate and dipentaerythritol fatty acid ester.

A preferred optional component is ethyl cellulose (Ethocel). Ethyl cellulose generally is preferred for use at levels of about 5% and more preferably 1%.

Another preferred optional component is silica. Silica is generally preferred for use at levels of from about 1% and about 5%.

Hypoallergenic compositions can be made from the liquid crystal, wax, oil and colors herein. These lipsticks should not contain fragrances, flavor oils, lanolin, sunscreens, particularly PABA, or other sensitizers or potential sensitizers and irritants.

The compositions of the present invention can also be made into long lasting or non-transferable cosmetic compositions. Detailed discussions of such lipsticks are found in Japanese Patent Publication Hei No. 6-199630 and European Patent Application 748622, both of which are herein incorporated by reference in their entirety.

Additional optional materials that can be incorporated in the compositions of the present invention can be found in PCT application WO 97/39733, to Oblong et al.

METHODS OF MANUFACTURING

The present invention encompasses methods of preparing stable cosmetic compositions comprising vitamin B_3 compounds. Conventional formulation and mixing techniques can be used and generally comprise dissolving vitamin B_3 compounds in a polar solvent and adding the solution to a hydrophobic base composed of an emollient component, and a stabilizing system comprising a solidifying agent and a surfactant, yielding a cosmetic composition comprised as described above. In a preferred embodiment, this invention provides a method of improving the skin penetration of vitamin B_3 compounds, especially in lips and improving product stability. Conventional formulation and mixing techniques are described in detail in Harry's Cosmeticology, pp. 119-141 and 314-354 (J.B. Wilkinson and R.J. Moore 7th ed 1982). and Cosmetics: Science and Technology, pp. 1-104 and 307-422 (M.S. Balsam and E. Sagarin 2nd ed 1972), both of which are herein incorporated by reference in their entirety.

METHODS OF USE

The cosmetic compositions of the present invention are ideally suited for use in treating the skin and lips, especially in the form of a lipstick or lip balm for applying to the lips a permanent or semi-permanent color, ideally with a gloss or luster finish. The cosmetic compositions can also be used in treating the skin and/or lips with a skin care agent for protection against exposure to adverse weather, including the wind and the rain, dry and/or hot environments, environmental pollutants (e.g., ozone, smoke, and the like), or exposure to excessive doses of sunlight. The compositions are also useful in providing sun protection, moisturizing and/or conditioning for the hair and skin, improved skin feel,

regulating skin texture, reducing fine lines and wrinkles, reducing oily shine on hair or skin, skin lightening and reducing skin or hair odor.

The cosmetic composition can, accordingly, be applied to the skin and/or lips in the traditional manner using a convenient holder or applicator to provide a decorative and/or protective film thereto.

EXAMPLES

The cosmetic formulations illustrated in Examples I-X illustrate specific embodiments of the cosmetic compositions of the present invention, but are not intended to be limiting thereof. Other modifications can be undertaken by the skilled artisan without departing from the spirit and scope of this invention. These exemplified embodiments of the cosmetic compositions of the present invention provide improve the skin penetration of the vitamin B_3 compound as well as improve the stability of the cosmetic composition.

All exemplified compositions can be prepared by conventional formulation and mixing techniques. Component amounts are listed as weight percents and exclude minor materials such as diluents, filler, and so forth. The listed formulations, therefore, comprise the listed components and any minor materials associated with such components.

Example I-Lipstick Composition

Ingredient	Weight %
Castor Oil	18.5
Isopropyl palmitate	11.6
Caprylic/capric/isostearic/adipic triglyceride	7.0
Lanolin	7.0
Red 21 Aluminum Lake	7.0
Candelilla wax	6.6
Propylene glycol myristyl ether acetate	6.0
Caprylic/capric triglyceride	5.8
Glycerol	5.0
Water	5.0
Niacinamide	1.0
Titanium dioxide	4.7
Beeswax	4.1
Monoglyceride	3.5
Lanolin oil	2.5
Ozokerite wax	2.5
Phospholipid (soybean lecithin)	1.0
Polybutene	0.8
Carnauba wax	0.4

The above ingredients are added to a stainless steel vessel equipped with a heating source. The ingredients are heated to about 85°C and mixed until a homogeneous. This mixture is then poured into a mold and cooled to room temperature.

The lipstick is applied to the lips to provide color, moisturization and improved skin penetration of the niacinamide.

Example II- Lipstick Composition

Ingredient	Amount (weight percent)
Carnauba	1.50
Ozokerite	6.00
Candelillia	4.00
Hydrogenated Vegetable Oil	5.00
Acetylated Lanolin	4.00
Isopropyl Isostearate	11.90
Isostearic Acid	10.00
Propylparaben	0.10
Cetyl Ricinoleate	10.00
Ascorbyl Palmitate	1.00
Silica L-700	1.00
Polybutene	2.00
Petrolatum	5.50
Association Structure Phase	
Sucrose Monooleate	14.00
Niacinamide	2.00
Glycerine	12.00
Pigment	9.00

The ingredients for the Association Structure Phase, except for the pigments, are mixed until association structures are formed. Once the association structures are formed, the pigments are added and milled on a three roll mill. The mixture is then mixed with the other ingredients and mixed until a homogeneous mixture. (Or, alternatively, the above components are added and mixed together at the same time.) This mixture is heated to 85°C and then poured into a mold at room temperature.

The lipstick is applied to the lips to provide color, moisturization and improved skin penetration of the niacinamide.

Example III-Lipstick Composition

Ingredient	Amount (weight percent)
Carnauba	1.50
Ozokerite	6.00
Candelillia	4.00
Hydrogenated Vegetable Oil	9.00
Isopropyl Palmitate	9.40
Isostearic Acid	11.50
Acetylated Lanolin	4.00
Propylparaben	0.10
Cetyl Ricinoleate	10.00
Ascorbyl Palmitate	1.00
Silica L-700	1.00
Polybutene	2.00
Petrolatum	5.50

Association Structure	
Phase	
Sucrose Monooleate	12.00
Niacinamide	2.00
Glycerine	12.00
Pigment	9.00

The composition is prepared and used as in Example II.

Example IV-Lipstick Composition

Ingredient	Amount (weight percent)
Carnauba	1.50
Ozokerite	5.50
Candelillia	4.00
Hydrogenated Vegetable Oil	8.50
Acetylated Lanolin	4.00
Propylparaben	0.10
Cetyl Ricinoleate	10.00
Ascorbyl Palmitate	1.00
Polybutene	2.00
Polysiloxane Copolymer[1]	5.97
Petrolatum	5.97
Anhydrous Lanolin	5.97
Association Structure Phase	
Lecithin	22.95
Niacinamide	2.50
Panthenol	1.00
Glycerine	6.00
Pigment	9.00
water	4.04

[1] #1154-141-1, supplied by GE Silicones.

The composition is prepared as in Example II.

Example V-Antiperspirant Gel Stick

Ingredient	Amount (weight percent)
N-Lauroyl-L-glutamic acid-di-n-butyl amide[1]	4
12-hydroxystearic acid	2
water	2.0
Niacinamide	2
Lecithin	0.1
Light mineral oil[2]	21.1
Diisopropyl Sebacate[3]	40.8
Aluminum Zirconium	25
Talc	3

[1]GP-1 supplied by Ajinomoto, Inc.
[2]Benol White Mineral Oil supplied by Witco Chemical Corp.
[3]Schercemol DIS supplied by Scher Cherfficals Inc.

In a stainless steel vessel, niacinamide is dissolved in water and combined with lecithin to form the association structures. Separately, the gelling agent and the liquid base material are combined into a vessel equipped with a heat source. Heat the mixture to between about 80°C and about 130°C with stirring, until the mixture forms a homogeneous, molten solution. Preferably, the homogeneous, molten solution is allowed to cool to a mixing temperature; typically between about 65°C and 120°C. (Alternatively, the mixture may simply be heated to the mixing temperature until the mixture forms a homogeneous, molten solution. This alternative method, however, typically takes longer than heating at high temperatures and then cooling.) Add the niacinamide mixture, antiperspirant active and other ingredients, such as fragrances and colors, into the homogeneous, molten solution in the above vessel with stirring. Allow the mixture to cool until it begins thickening and then pour the mixture into containers allowing them to cool to ambient temperature. (Although not preferred, the antiperspirant active may alternatively be added along with the gelling agent and the liquid base material in the first step.)

An antiperspirant composition, comprised as above, is applied to the underarm area of a human subject, and reduces the perspiration in the applied area and improves odor in this area.

Example VI-Solid Antiperspirant Stick

Ingredient	Amount (weight percent)
Stearyl Alcohol	9.8
Niacinamide	0.1
Lecithin	1.0
Butylene Glycol	1.2
Hydrogenated Castor Oil-mp 86 degrees C.	4.0
Aluminum Chlorohydroxide	40.0
Isopar "V"[1]	42.9
Fragrance	1.0

[1](Isopar "V" Avg. Mol. Wt. 197 B.P. Range, 255-301 degrees C.) -

In a stainless steel vessel, niacinamide is dissolved in butylene and combined with lecithin to form the association structures. Separately , the isoparaffin liquids, the water-insoluble liquid emollients, the surface active agent, and the water-insoluble waxes are combined and heated to a temperature sufficient to form a solution of these materials, followed by the addition of the active astringent antiperspirant salts with gentle agitation. Following addition of the niacinamide mixture and salts, other optional ingredients such as talc may then be added and mixed until a homogenous suspension is formed. The suspension is cooled to a temperature above the solidification point and is then poured into suitable containers.

An antiperspirant composition, comprised as above, is applied to the underarm area of a human subject, and reduces the perspiration in the applied area and improves odor in this area.

Example VII-Antiperspirant Cream

Ingredient	Amount (weight percent)
cyclomethicone (D5)	41.5

dimethicone (350 cs)	4.0
Cab-O-Sil HS-5[1]	4.0
Microthene FN510[2]	6.0
Natrosol[3]	2.0
Lecithin	0.5
Niacinamide	0.5
Glycerin	3.0
iso-eicosane[4]	13.0
Reach AZ[5]	26.7
fragrance	0.8

[1]Colloidal silica thickening material, sold by Cabot Corporation. -

[2]Low density polyethylene powder, sold by U.S.I. Chemicals. -

[3]Hydroxyethylcellulose, sold by Hercules, Inc. -

[4]2, 2, 4, 4, 6, 6, 8, 8-dimethyl-10-methylundecane, obtained from Permethyl Corporation, Frazier, PA. -

[5]Zirconium-aluminum-glycine hydroxychloride complex, particulate antiperspirant active material, sold by Reheis Chemical Company. -

The cyclomethicone dimethicone, iso-eicosane and perfume are added to a stainless steel mixing vessel. The Cab-O-Sil is then added, followed by the Microthene and Natrosol and, finally, the antiperspirant active. The composition is thoroughly stirred after addition of each particulate material.

The composition is then milled, using a Black & Decker Die Grinder (Model 4420, type 4) with a 6.35 cm diameter Cowles dispersing blade at approximately 6,000 rpm, for approximately 5 minutes. The penetration force value of the milled composition is approximately 300 grams at 25o C. and 50% relative humidity.

An antiperspirant cream formulation, comprised as above, is applied to the underarm area of a human subject, and reduces the perspiration in the applied area and improves odor in this area.

Example VIII-Mascara

Ingredient	Amount (weight percent)
Carnauba Wax	3.00
Glyceryl Monostearate[1]	7.50
White Beeswax	3.75
C18-C36 Triglycerides[2]	5.50
Hydrogenated Glycerol Rosinate[3]	0.15
Propylparaben	0.10
Paraffin Wax 118/125	2.25
Paraffin Wax	2.25
Lecithin[4]	2.25
Stearic Acid 3X	4.00
Oleic Acid	0.75
Triethanolamine	1.25
Potassium Cetyl Phosphate[5]	1.00
Shellac, NF	3.00

Triethanolamine	0.47
Trisodium EDTA	0.10
Black Iron Oxide	7.00
Dimethicone	0.20
Methylparaben	0.20
Ethylparaben	0.15
Phenoxyethanol	0.80
Ethyl Alcohol 40B, 190 proof	4.00
Diazolidinyl Urea	0.20
Deionized Water	44.78
dl-Panthenol	0.35
niacinamide	5.00
Total	100.00

[1] Available as Emerest 2400 available form Henkel/Emery -
[2] Available as Syncrowax HGL-C available from Croda, Inc. -
[3] Available as Foral 105 available from Hercules, Inc. -
[4] Available as Centrolex F available from Central Soya, Inc. -
[5] Available as Amphisol K available from Givaudan -

The waxes and fats are mixed in a vessel equipped with a heating source. The waxes and fats are heated and mixed at low speed using a conventional blender to liquify the mixture. The mixing is continued until the mixture is homogeneous. To the homogenous mixture is added the pigments. The mixing rate is increased to high and the pigments are mixed into the mixture for about 30-35 minutes until uniformly dispersed. The mixing is continued while adding emulsifiers.

In a second vessel equipped with a heating source is added water followed by the niacinamide, lecithin and any other water-dispersable components. The mixture is heated and mixed to a temperature of from about 80-95°C. Additional water is added as necessary to account for water loss.

The aqueous and lipophilic mixtures are combined and mixed using a dispersator type mixer. Mixing is continued until the mixture cools to a temperature of from about 65-70°C. Preservatives are added with mixing, allowing the mixture to cool further to 45-47°C. Any remaining components are added with mixing. The combined mixture is cooled to a temperature above the solidification point and is then poured into suitable containers.

The mascara composition is applied to the lashes and/or eyebrows to provide softening, moisturization and conditioning.

Example IX-Mascara

Ingredient	Amount (weight percent)
Carnauba Wax	2.00
Glyceryl Monostearate[1]	8.50
White Beeswax	3.25
C17-C36 Triglycerides[2]	5.50
Hydrogenated Glycerol Rosinate[3]	0.15
Propylparaben	0.10
Paraffin Wax 118/125	2.25

Paraffin Wax	2.25
Lecithin[4]	2.50
Stearic Acid 3X	4.00
Oleic Acid	0.75
Triethanolamine	2.00
Potassium Cetyl Phosphate[5]	1.00
Deionized Water	41.03
Shellac, NF	3.00
Triethanolamine	0.47
PVP/VA Copolymer[6]	0.25
Black Iron Oxide	10.00
Simethicone	0.20
Methylparaben	0.20
Ethylparaben	0.15
Phenoxyethanol	0.80
Ethyl Alcohol 40B, 190 proof	4.00
Diazolidinyl Urea	0.20
Trisodium EDTA	0.10
dl-Panthenol	0.35
niacinamide	5.00
Total	100.00

[1] Available as Emerest 2400 available form Henkel/Emery -
[2] Available as Syncrowax HGL-C available from Croda, Inc. -
[3] Available as Foral 105 available from Hercules, Inc. -
[4] Available as Centrolex F available from Central Soya, Inc.
[5] Available as Amphisol K available from Givaudan -
[6] Available as PVP/VA S-630 available from ISP -

The mascara is prepared and used as in Example VIII.

Example X-Lipsticks

INGREDIENT	Ex. Xa WT. %.	Ex. Xb WT. %.
Polybutene	4.536	4.536
Lanolin Oil	18.342	18.342
Octoxyglyceryl Behenate	18.342	18.342
Stearyl heptanoate	8.856	8.856
Jojoba oil	8.856	8.856
castor oil	19.28	24.08
Butylated hydroxytoluene	0.054	0.054
Butylated hydroxyanisole	0.054	0.054
Microcrystalline Wax	6.84	6.84
Polyethylene 500	6.84	6.84
Association Phase		
Lecithin	0.475	0.475
Water	6	1.2
Niacinamide	1	1
Cholesterol	0.475	0.475
dicetyl phosphate	0.05	0.05

In a suitable vessel, the castor oil, polybutene, lanolin oil, octoxyglyceryl behenate, stearyl heptanoate, jojoba oil, butylated hydroxytoluene, butylated hydroxyanisole, microcrystalline wax, polyethylene 500 are added to a vessel equipped with a heat source and heated to a temperature of from about 100-110°C to form a melt. The melt is mixed until homogeneous. Separately, the niacinamide is dissolved in the polar solvent (i.e, the water). The niacinamide solution is then mixed with lecithin, cholesterol and dicetyl phosphate to form association structures. The niacinamide/association structure mixture is then added to the castor oil containing mixture and mixed until uniform. The mixture is deaerated by vacuum and poured into the appropriate mold. The mixture is cooled to ambient temperature and incorporated into the appropriate package.

The lipstick is applied to the lips to provide color, moisturization and improved penetration of the niacinamide.

Example XI-Solid Compact Emulsion

Ingredient	%W/W
Part A	
Cyclomethicone 245	14.00
Cyclo/ dimethicone copolyol (DC5225C)[1]	15.00
Isononyl Isononanoate	3.00
Abil Quat 3272	1.00
Part B	
Laureth 7 (Rhodasurf L-790)[2]	0.50
Propylparaben	0.25
Part C	
MT-600	5.07
Tronox	4.06
Glycerin	4.53
Black iron oxide slurry	0.10
Yellow Iron Oxide slurry	1.87
Red Iron Oxide slurry	0.33
Zinc Oxide	5.00
Niacinamide	5.00
Lecithin	1.00
Methylparaben	0.12
Deionized water	27.33
Part D	
Dimethicone treated Talc	5.00
Polytrap	1.34
Ethylene Acrylic Acid Copolymer (EA-209)[3]	2.00
Ozokerite wax	3.50

[1] Available from Dow Corning
[2] Available from Rhone Poulenc
[3] Available from Rhone Poulenc

In a suitable vessel, the ingredients of Part C are combined and milled using a Silverson L4R at high speed (preferably about 9000-10000 rpm) with 1" disintegrating screen for at least ½ hour or until the mixture is uniform. In a separate vessel, the ingredients of Part A are combined and mix using a Silverson

L4R at about 3000rpm with 2" emulsor screen. The ingredients of Part B are combined separately and, before the propylparaben is completely dissolved, Part B is added to Part A using a Silverson L4R at about 3000-4000 rpm with 2" emulsor screen. Part C is slowly added the Parts A and B with mixing using a Silverson L4R at about 6000rpm with 2" emulsor screen. Mixing is continued until mixture is uniform. Part D is added maintaining adequate turnover (i.e., using a blending speed of about 6000-8000 rpm) and then heated to a temperature of about 80°C. The oxokerite wax is added to the heated mixture with mixing until mixture is uniform. The mixture is deaerated by vacuum and poured into the appropriate mold. The mixture is cooled to ambient temperature and incorporated into the appropriate package.

The solid compact emulsion is applied to the skin to reduce fine lines and texture of skin as well as reduce oily shine.

Example XII-Long Lasting Cosmetic Emulsion

. (Association Structure Example)

A. An admixture (Part A) is prepared by combining in a suitable vessel the following ingredients:

INGREDIENT	WT. %.
MQ Resin[1]	43.7
PM99A[2]	56.3

[1] Trimethylsiloxysilicate available from GE.

[2] Isododecane available from Presperse.

The admixture is mixed using conventional mixing techniques until the MQ Resin is dissolved.

Processing:

B. An admixture (Part B) is prepared by combining in a suitable vessel the following ingredients:

INGREDIENT	WT. %.
SE30 Silicone Gum[1]	50.0
PM99A	50.0

[1] Available from GE.

The admixture is mixed using conventional mixing techniques until the SE30 Silicone Gum is dissolved.

C. A cosmetic emulsion composition containing Part A and Part B is prepared by combining the following ingredients:

INGREDIENTS	WT. %
Part A	36.89
Part B	19.00
Pigments	10.00
PM99A	1.41

Propylparaben	0.20
Bentone ISD	15.00
Water	10.00
Niacinamide	5.00
Lecithin[1]	2.00
Laponite XLS	0.5

[1] Available under the tradename Centrolex F by Central Soya

In a suitable vessel, the admixture of Part A along with the pigments, propylparaben and PM99A are combined and mixed using a Ultra Turrax T25 homogenizer at about 8,000 rpms. for about 10 minutes or until the cosmetic mixture is uniform (taking care not to ignite the PM99A). The Bentone ISD added to the cosmetic mixture with mixing at about 8, 000 rpms. until the mixture is uniform.. The water, niacinamide and lecithin are mixed together in a separate vessel to form association structures and then added to the cosmetic mixture with stirring. The Laponite XLS is added to the mixture and mixing using a Ross homogenizer at about 3,500rpms until uniform. The admixture of Part B is added to the cosmetic mixture and mixed initially at high shear, preferably 1600 rpms., to facilitate dispersion using an IKA mixer. Once sufficient dispersion is achieved, the mixer speed is reduced, preferably to about 1,000 rpms., and the cosmetic mixture is allowed to mix until uniform. The cosmetic mixture is then poured into a suitable container and tightly capped for storage, preferably at room temperature.

The cosmetic emulsion composition is applied to impart color to the skin, improve skin texture and provide improved skin penetration of the niacinamide..

WHAT IS CLAIMED IS:

1. A topical cosmetic composition, useful for improving skin penetration of vitamin B_3 compounds, characterized in that the composition comprises:

a) from 0.01% to 50%, by weight of the composition, of a vitamin B_3 compound;

b) from 1% to 90%, preferably from 1% to 80%, by weight of the composition, of an emollient component comprising from 0.1% to 100%, preferably from 1% to 90%, by weight of the emollient component, of an oil that is liquid at ambient temperature;

c) from 0.1% to 80%, by weight of the composition, of a stabilizing system, which stabilizing system comprises;

i) from 0.1% to 90%, by weight of the stabilizing system, of a solidifying agent; and

ii) from 0.01% to 30%, by weight of the stabilizing system, of a surfactant, wherein the surfactant has a Krafft point at or below $20^{o}C$ and forms association structures; and;

d) from 0.01% to 90%, by weight of the composition, of a polar solvent.

2. A cosmetic composition according to Claim 1, wherein the vitamin B_3 compound is selected from niacinamide, derivatives of niacinamide, non-vasodilating esters of nicotinic acid, and combinations thereof, preferably niacinamide, tocopherol nicotinate, and combinations thereof, more preferably niacinamide.

3. A cosmetic composition according to Claims 1 or 2, wherein the association structure is selected from the group consisting of cylindrical reverse micelles, lyotropic liquid crystals and mixtures thereof, preferably is selected from unilamellar vesicles, multilamellar vesicles, cylindrical reverse micelles, hexagonal liquid crystals, cubic liquid crystals, lamellar liquid crystals and mixtures thereof, more preferably is selected from the group consisting of lamellar liquid crystals, reverse hexagonal liquid crystals and mixtures thereof.

4. A cosmetic composition according to Claim 3, wherein the reverse micelles aggregate to form networking spherical structures, elongated structures, cylindrical structures, vesicles, filament structures, or mixtures thereof.

5. A cosmetic composition according to any of Claims 1 to 4, wherein the association structure comprises from 0.1% to 75%, preferably from 5% to 65% of the cosmetic composition.

6. A cosmetic composition according to any of Claims 1 to 5, wherein said polar solvent comprises from 10% to 80% of the association structure and wherein said surfactant comprises from 30% to 80% of the association structure.

7. A cosmetic composition according to any of Claims 1 to 6, wherein the polar solvent is selected from the group consisting of water, glycerine, propylene glycol, butylene glycol, hexylene glycol, alcohol, panthenol and mixtures thereof.

8. A cosmetic composition according to any of Claims 1 to 7, wherein the oil is selected such that at least 99% of the types of oils used have solubility parameters which do not differ by more than from 0.1 to 1.5.

9. A cosmetic composition according to any of Claims 1 to 8, which composition is further characterized in that it comprises from 0.1% to 90%, preferably 1% to 35%, by weight of the composition, of a water-insoluble color component.

10. A method of improving the skin penetration of vitamin B_3 compounds by applying to the skin a safe and effective amount of the composition in Claim 1.

INTERNATIONAL SEARCH REPORT

Inter nal Application No
PCT/US 00/03463

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K7/48 A61K7/027

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 95 11000 A (THE PROCTER & GAMBLE COMPANY) 27 April 1995 (1995-04-27) the whole document & US 5 843 407 A	1-10
Y	WO 98 52530 A (THE PROCTER & GAMBLE COMPANY) 26 November 1998 (1998-11-26) page 1, line 1 -page 22, line 16 page 24, line 21 -page 32, line 7 example 1	1-10
A	EP 0 539 215 A (STAFFORD-MILLER LTD. ET AL.) 28 April 1993 (1993-04-28) claims 1,2	

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
30 May 2000	07/06/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Alvarez Alvarez, C

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INTERNATIONAL SEARCH REPORT

Inter nal Application No
PCT/US 00/03463

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 496 827 A (JAY PATRICK) 5 March 1996 (1996-03-05) abstract column 3, line 57 - line 58	

INTERNATIONAL SEARCH REPORT

...formation on patent family members

Inter ...nal Application No
PCT/US 00/03463

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9511000 A	27-04-1995	AU 697809 B	15-10-1998
		AU 8014994 A	08-05-1995
		CA 2173104 A	27-04-1995
		CN 1135171 A	06-11-1996
		CZ 9601107 A	14-08-1996
		EP 0725620 A	14-08-1996
		EP 0950392 A	20-10-1999
		JP 9503785 T	15-04-1997
		US 5843407 A	01-12-1998
WO 9852530 A	26-11-1998	US 5968528 A	19-10-1999
		AU 7074898 A	11-12-1998
		EP 0983047 A	08-03-2000
EP 539215 A	28-04-1993	AT 169228 T	15-08-1998
		AU 658681 B	27-04-1995
		AU 2726692 A	29-04-1993
		CA 2081269 A	24-04-1993
		DE 69226491 D	10-09-1998
		DE 69226491 T	14-01-1999
		ES 2119800 T	16-10-1998
		JP 2671248 B	29-10-1997
		JP 6128176 A	10-05-1994
		NZ 244862 A	26-07-1995
		US 6017520 A	25-01-2000
US 5496827 A	05-03-1996	NONE	